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| APPLICATION NO.   | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|-------------|----------------------|---------------------|------------------|
| 09/877,374  | 06/08/2001  | Jeffrey C. Rapp      | AVI-007N            | 2448             |
| 26739   | 7590        | 09/19/2007           | EXAMINER            |                  |
| AVIGENICS, INC.<br>111 RIVERBEND ROAD<br>ATHENS, GA 30605 |             |                      | TON, THAIAN N       |                  |
|   |             |                      | ART UNIT            | PAPER NUMBER     |
|   |             |                      |                     | 1632             |
|   |             |                      | MAIL DATE           | DELIVERY MODE    |
|   |             |                      | 09/19/2007          | PAPER            |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

|                              |                                  |                         |
|------------------------------|----------------------------------|-------------------------|
| <b>Office Action Summary</b> | <b>Application No.</b>           | <b>Applicant(s)</b>     |
|                              | 09/877,374                       | RAPP, JEFFREY C.        |
|                              | <b>Examiner</b><br>Thaian N. Ton | <b>Art Unit</b><br>1632 |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) Responsive to communication(s) filed on 27 June 2007.
- 2a) This action is FINAL.                    2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) Claim(s) 1-5,9-29,62-70 and 72 is/are pending in the application.
  - 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 1-5,9-29,62-70 and 72 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.
  - Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
  - Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a) All    b) Some \* c) None of:
    1. Certified copies of the priority documents have been received.
    2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
    3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

|  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 5) <input type="checkbox"/> Notice of Informal Patent Application |
|  | 6) <input type="checkbox"/> Other: _____                          |

## DETAILED ACTION

Applicants' Remarks, filed 6/27/07, have been entered. Applicants filed no claim amendments with their remarks.

Claims 1·5, 9·29, 62·70, and 72 are pending and under current examination.

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1·5, 9·17, 19·29, 62 and 63 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Ditullio *et al.* when taken with Sanders *et al.* in further view of Mohammed *et al.* and in further view of Michael *et al.*

*Applicants' Arguments.* Applicants' argue that the combination of cited art fails to render the claimed invention obvious, because Ditullio do not indicate that the manipulated blastodermal cells express the introduced transgene. Applicants argue that there is no indication that the blastoderm cells that were "manipulated" *in vitro* to contain a transgene were contemplated to produce an immunoglobulin polypeptide, and that this cell could have been manipulated to contain a desired coding sequence to express and secrete a coding sequence product for the purpose of purification. Additionally, Applicants argue that there is no indication of success that Ditullio produces a transgenic bird that produces antibodies, or any other protein. Applicants argue that Ditullio only show transgene DNA in heart, liver, and kidney tissue, but no transgene expression is shown in bird tissue. Applicants argue that although Ditullio discloses various aspects of gene expression, there is no evidence that heterologous gene expression in the transgenic bird, including oviduct tissue.

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*Response to Arguments.* These arguments have been fully considered, but are not persuasive. Ditullio is not used to show the transfection of oviduct cells, because they teach transfection of blastoderm cells, which are not oviduct cells. Applicants' arguments, which are directed to Ditullio's production of transgenic birds, are not within the scope of the claimed invention, which is directed to an *in vitro* method of transfecting avian oviduct cells. The Examiner further notes that Ditullio states that PCR analysis of necropsy samples showed that one of the four chicks "had detectable levels of the transgene in its reproductive organs". It is unclear if reproductive organs include oviduct tissue, for example. Regardless, Applicants' arguments are not found to be persuasive because Applicants' citation of Ditullio's lack of transgene expression in bird tissue, and in particular, oviduct tissue, is not within in the scope of the claimed invention, because transgenesis requires expression of a transgene *in vivo*, whereas Applicants' claims are directed to *in vitro* embodiments. Ditullio's *in vivo* results fail to provide any prediction of whether or not an avian oviduct cell can be transfected to produce an antibody, *in vitro*. Additionally, the Examiner has provided evidence that shows that oviduct cells can readily be transfected with vectors to express heterologous genes (see Sanders *et al.*) and that human antibodies can be expressed in bird cells (see Mohammed and Michael).

*Applicants' Arguments.* Applicants argue that Sanders demonstrates that production of a well-known reporter protein in an oviduct cell may be possible to analyze gene regulatory sequences, but this is not indicative of the production of useful antibodies is feasible in transfected oviduct cells. Applicants argue that antibodies are more complex, with regard to glycosylation, than CAT (which was expressed by Sanders), and additionally, Sanders does not disclose heterologous production of any protein product which is intended to be useful, outside the context of being inside the oviduct cell, where the protein can perform a specific function, they do not disclose or contemplate purification of proteins, and are, as such, not

related to the claimed invention. See pages 3-4 of the Response. Applicants argue that although Mohammad teach utilizing DT40 cell lines that can secrete recombinant human antibodies, their work does not suggest or teach the production of antibodies from oviduct cells, and moreover, Mohammad is directed to injection of recombinant DT40 cells in chickens for purposes of producing the antibody in the chicken, not for the production and isolation or purification of the antibodies such as the instant invention. See page 4 of the Response. Applicants argue that although Michael teach isolating antibodies from chicken cells (DT40), they do not teach heterologous monoclonal antibodies, and the passages recited in the prior Office action do not relate to making a transgenic chicken, or making antibodies in oviduct cells in cultures. See pages 4-5 of the Response. Applicants argue that the Examiner does not provide a suggestion or motivation in the art for the skilled artisan to combine the necessary features to arrive at the claimed invention, and that the Examiner “steps through various references citing components of the references that when taken together allegedly constitute all the features of the claims.” See page 5 of the Response.

**Response to Arguments.** In response to Applicants’ arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In the instant case, the Examiner relies upon the combination of references to arrive at the claimed invention. Additionally, the Examiner notes that, that KSR forecloses the argument that a specific teaching, suggestion, or motivation is required to support a finding of obviousness. See the recent Board decision *Ex parte Smith*, --USPQ2d--, slip op. at 20, (Bd. Pat. App. & Interf. June 25, 2007) (citing KSR, 82 USPQ2d at 1396) (available at <http://www.uspto.gov/web/offices/dcom/bpai/prec/fd071925.pdf>).

In the instant case, Ditullio teaches *in vitro* methods of producing heterologous antibodies. Sanders teach that tubular gland cells are capable of producing heterologous proteins, and Mohammed and Michael provide sufficient teachings for standard methods of isolation of immunoglobulins from cultured cells. Thus, it would have been obvious to one of ordinary skill in the art to apply the *in vitro* methods of Ditullio, with cells, such as those taught by Sanders, to produce and purify antibodies, as taught by Mohammed and Michael to attempt to optimize the isolation of antibodies directly from cultured cells, such as oviduct cells, which would be more efficient than producing a transgenic bird, and further, the cytomegaloviral promoter is a well-known and well-characterized promoter that would allow for optimal levels and patterns of gene expression, that utilizing an IRES element would facilitate expression of multiple genes, and that viral transduction is an efficient way to deliver a construct to a cell.

Accordingly, this rejection is maintained.

Claim 18 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Ditullio *et al.* when taken Sanders, in further view of Mohammed, and in further view of Michael *et al.* as applied to claim 1-5, 9-17, 19-29, 62 and 63 above, and further in view of Larocca *et al.*.

Applicants provide no substantive arguments with regard to this rejection, other than the traversal of the rejection, as it applies to the arguments addressed above. Accordingly, this rejection is maintained.

Claims 64-69, 70 and 72 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Ditullio *et al.* when taken Sanders, in further view of Mohammed, and in further view of Michael *et al.* as applied to claims 1-5, 9-17, 19-29, 62 and 63 above, and further in view of Ling *et al.* and Najarfian *et al.*

Applicants provide no substantive arguments with regard to this rejection, other than the traversal of the rejection, as it applies to the arguments addressed above. Accordingly, this rejection is maintained.

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*Conclusion*

No claim is allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Thaian N. Ton whose telephone number is (571) 272-0736. The Examiner can normally be reached on Monday through Thursday from 7:00 to 5:00 (Eastern Standard Time). Should the Examiner be unavailable, inquiries should be directed to Peter Paras, SPE of Art Unit 1632, at (571) 272-4517. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the Official Fax at (571) 273-8300. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Thaian N. Ton/  
**Primary Examiner**  
**Art Unit 1632**